Devi, S.
09/623038

18mar05 14:44:27 User219783 Session D2083.2

SYSTEM:OS - DIALOG OneSearch
File 65:Inside Conferences 1993-2005/Mar W2
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File 440:Current Contents Search(R) 1990-2005/Mar 18
(c) 2005 Inst for Sci Info
File 348:EUROPEAN PATENTS 1978-2005/Feb W04
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File 357:Derwent Biotech Res. _1982-2005/Mar W3
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File 113:European R&D Database 1997
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Set Items Description
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Set	Items	Description
S1	0	1B6E12H9 ← Antibody
S2	209	AU=(CARLONE, G? OR CARLONE G?) - Author(s)
S3	250	AU=(ADES, E? OR ADES E?)
S4	795	AU=(SAMPSON, J? OR SAMPSON J?)
S5	30	AU=(THERPE, J? OR THERPE J? OR THARPE J? OR THARPE, J?)
S6	19	AU=(ZEILER, J? OR ZEILER J?)
S7	56	AU=(WESTERINK, M? OR WESTERINK M?)
S8	2	S2 AND S3 AND S4 AND S5 AND S6 AND S7
S9	72	S2 AND (S3 OR S4 OR S5 OR S6 OR S7)
S10	53	S3 AND (S4 OR S5 OR S6 OR S7)
S11	19	S4 AND (S5 OR S6 OR S7)
S12	2	S5 AND (S6 OR S7)
S13	4	S6 AND S7
S14	25	(S9 OR S10 OR S11) AND (MOAB? ? OR MAB? ? OR MONOCLONAL)
S15	26	S8 OR S12 OR S13 OR S14
S16	13	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

16/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

15791665 Document Delivery Available: 000181566700009 References: 31
TITLE: Inhibition of pneumococcal adherence to human nasopharyngeal epithelial cells by anti-PsaA antibodies
AUTHOR(S): Romero-Steiner S (REPRINT); Pilishvili T; **Sampson JS**; Johnson SE; Stinson A; **Carlone GM**; **Ades EW**
AUTHOR(S) E-MAIL: SSteiner@cdc.gov
CORPORATE SOURCE: Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, MS A-36,1600 Clifton Rd/Atlanta//GA/30333 (REPRINT); Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, /Atlanta//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 2003, V10, N2 (MAR), P246-251
GENUINE ARTICLE#: 655RP
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 1071-412X

Searcher : Shears 571-272-2528

LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The role of pneumococcal (Pnc) surface adhesin A (PsaA) in the adherence of Streptococcus pneumoniae (pneumococcus) to host cells is not well defined. We examined the effect of anti-PsaA antibodies in an inhibition of adherence assay using Detroit 562 nasopharyngeal human epithelial cells. Rabbit polyclonal (Pab) anti-recombinant PsaA (rPsaA) sera, a purified mouse **monoclonal** antibody (**MAb**) (**MAb** 6F62G8E12), and 22 healthy adult sera with known anti-PsaA IgG levels (obtained by enzyme-linked immunosorbent assay) were evaluated for their abilities to inhibit Pnc adherence to confluent monolayers (measured as percent reduction in CFU counts compared to those of uninhibited controls). Pnc adherence was dependent on capsular phenotype (no or low adherence for opaque strains). With an inoculum of 10(4) to 10(5) bacteria/well, the mean +/- standard deviation count in controls was 163 +/- 32 CFU/well for transparent strains. Low adherence was observed for a PsaA-minus mutant even at higher inoculum doses. Mean percent inhibitions of adherence with Pab and **MAb** were 54 and 50%, respectively. Adult sera showed inhibition in a dose-response fashion with a range of 98 to 8%, depending on the serum anti-PsaA antibody concentration. Absorption of Pab with rPsaA restored Pnc adherence to control levels. Absorption of sera with a PsaA-minus mutant did not result in a significant decrease (P >0.05) of inhibition of adherence activity. Additionally, nearly 100% of Pnc adherence was inhibited by lipidated rPsaA at 2.5 mug/ml. Our data support the argument that PsaA is an adhesin that mediates Pnc adherence to human nasopharyngeal cells. This functional assay may be useful in evaluating antibodies elicited in response to PsaA vaccination.

16/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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13586721 Document Delivery Available: 000174457600039 References: 52
TITLE: Newly characterized species-specific immunogenic Chlamydophila pneumoniae peptide reactive with murine **monoclonal** and human serum antibodies
AUTHOR(S): Marston EL (REPRINT); James AV; Parker JT; Hart JC; Brown TM; Messmer TO; Jue DL; Black CM; **Carlone GM; Ades EW; Sampson J**
AUTHOR(S) E-MAIL: EMARSTON@CDC.GOV
CORPORATE SOURCE: CDCP, Natl Ctr Infect Dis,US Dept Hlth & Human Serv, /Atlanta//GA/30333 (REPRINT); CDCP, Natl Ctr Infect Dis,US Dept Hlth & Human Serv, /Atlanta//GA/30333; CDCP, US Dept HHS, /Atlanta//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 2002, V9, N2 (MAR), P446-452
GENUINE ARTICLE#: 532EA
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 1071-412X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: A **monoclonal** antibody (**MAb**) directed against an unknown Chlamydophila pneumoniae epitope has been characterized, and the respective peptide mimotope has been identified. A murine **MAb**

specific for C. pneumoniae was used to select peptides from phage display libraries. The peptides identified from the phage display library clones reacted specifically with the respective target murine **MAb** and with human sera previously identified as having antibody titers to C pneumoniae. The selected peptide mimotope sequences tended to be composed of charged residues surrounding a core of hydrophobic residues. The peptide with the best binding could inhibit >95% of binding to the **MAb**, suggesting that the selected peptide binds the paratope of the respective **MAb**. The peptide reacted with human sera previously determined by microimmunofluorescence to have anti-C pneumoniae antibodies. The peptide was competitively competed with the **MAb** against Renografin-purified, sonicated C. pneumoniae in an enzyme-linked immunosorbent assay and with whole-cell C. pneumoniae in an indirect fluorescence assay format, demonstrating its potential utility in the development of diagnostics. The use of this novel peptide may allow investigators to establish standardized assays free from cross-reactive Chlamydia trachomatis and Chlamydophila psittaci epitopes and immunoreactivity.

16/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

13455012 References: 47
TITLE: Inhibition of pneumococcal carriage in mice by subcutaneous immunization with peptides from the common surface protein pneumococcal surface adhesin A
AUTHOR(S): Johnson SE (REPRINT); Dykes JK; Jue DL; **Sampson JS; Carlone GM; Ades EW**
AUTHOR(S) E-MAIL: sjohnson@cdc.gov
CORPORATE SOURCE: CDCP, Resp Dis Branch, Mailstop A36/Atlanta//GA/30333 (REPRINT); CDCP, Resp Dis Branch, /Atlanta//GA/30333; CDCP, Natl Ctr Infect Dis, /Atlanta//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: JOURNAL OF INFECTIOUS DISEASES, 2002, V185, N4 (FEB 15), P 489-496
GENUINE ARTICLE#: 517DM
PUBLISHER: UNIV CHICAGO PRESS, 1427 E 60TH ST, CHICAGO, IL 60637-2954 USA
ISSN: 0022-1899
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Pneumococcal surface adhesin A (PsaA), a common protein expressed on all 90 pneumococcal serotypes, is a vaccine candidate. Three anti-PsaA **monoclonal** antibody phage display-expressed monopeptides (15 mers), in various formulations as lipidated or nonlipidated multiantigenic peptides or as bi- or tripeptide constructs, were studied in a mouse nasopharyngeal carriage model to determine the inhibitory effect of induced antibodies on carriage of pneumococcal serotypes 2, 4, and 6B. Antibodies to each of the various peptides tested reduced carriage of the 3 serotypes. Reduction in carriage by nonlipidated multiantigenic peptide antibodies was highly variable (39%-94%; mean, 59%; standard deviation [SD], 20.2%); however, more-consistent results were observed in mice immunized with lipidated (56%-98%; mean, 69%; SD, 13.6%) and combination or bipeptide (55%-91%; mean, 76%; SD, 13.1%) formulations. These peptides are immunogenic, and their induced antibodies reduce carriage in mice. PsaA peptides demonstrate potential for being important new vaccines against

pneumococcal carriage, otitis media, and invasive pneumococcal disease.

16/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

11485754 References: 64
TITLE: Selection of an immunogenic and protective epitope of the PsaA protein of Streptococcus pneumoniae using a phage display library
AUTHOR(S): Srivastava N; **Zeiler JL**; Smithson SL; **Carlone GM**; **Ades EW**; **Sampson JS**; Johnson SE; Kieber-Emmons T; **Westerink MAJ (REPRINT)**
AUTHOR(S) E-MAIL: mwesterink@mco.edu
CORPORATE SOURCE: Med Coll Ohio, Dept Med, 3055 Arlington Ave/Toledo//OH/43614 (REPRINT); Med Coll Ohio, Dept Med, /Toledo//OH/43614; Med Coll Ohio, Dept Pathol, /Toledo//OH/43614; Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, /Atlanta//GA/30333; Univ Penn, Dept Pathol & Lab Med, /Philadelphia//PA/19104
PUBLICATION TYPE: JOURNAL
PUBLICATION: HYBRIDOMA, 2000, V19, N1 (FEB), P23-31
GENUINE ARTICLE#: 300ER
PUBLISHER: MARY ANN LIEBERT INC PUBL, 2 MADISON AVENUE, LARCHMONT, NY 10538 USA
ISSN: 0272-457X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Streptococcus pneumoniae is an important pathogen that causes disease in young and elderly individuals. The currently available polysaccharide vaccines have limited efficacy in those age groups most susceptible to pneumococcal infections. This study focuses on mapping the epitopes of a surface protein of S, pneumoniae by biopanning a 15 mer phage display library using 5 different **monoclonal** antibodies (**MAbs**) against the Pneumoccal surface adhesin A (PsaA). PsaA is a component of the bacterial cell wail that is highly species specific and is involved in bacterial adherence and virulence. Biopanning of the phage display library reveals three distinct epitopes on the PsaA protein, The sequence homology of these epitopes ranges from two to six amino acids when compared to the native PsaA protein type 2. Two of these epitopes have been evaluated for their immunogeneicity in mice. The peptide selected by the **MAbs** 8G12, 6F6, and 1B7 is referred to as the consensus peptide and is immunogenic in mice. Optimal anti-PsaA response is observed in mice immunized with 50 mu g of the consensus peptide complexed to proteosomes in 1:1 ratio. The anti-PsaA response is significantly lower than the response to the PsaA native protein. The peptide selected by **monoclonal** antibody 4E9 in its lipidated form is significantly protective in mice challenged with S, pneumoniae serotype 2 when compared to mice immunized with the native protein. These results show that the selected epitopes of PsaA protein are immunogenic and protective in mice. These epitopes need to be evaluated further as alternatives to currently available vaccines.

16/3,AB/5 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

11245786 References: 60
TITLE: Selection of an immunogenic peptide mimic of the capsular polysaccharide of Neisseria meningitidis serogroup A using a peptide display library
AUTHOR(S): Grothaus MC; Srivastava N; Smithson SL; Kieber-Emmons T; Williams DB; **Carlone GM; Westerink MAJ (REPRINT)**
AUTHOR(S) E-MAIL: mwesterink@mco.edu
CORPORATE SOURCE: Med Coll Ohio, Dept Pathol & Med, POB 10008/Toledo//OH/43699 (REPRINT); Med Coll Ohio, Dept Pathol & Med, /Toledo//OH/43699; Univ Penn, Dept Pathol & Lab Med, /Philadelphia//PA/19104; Ctr Dis Control, Resp Dis Branch, /Atlanta//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 2000, V18, N13 (JAN 18), P1253-1263
GENUINE ARTICLE#: 271NT
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The presently available meningococcal vaccine is poorly immunogenic in infants and fails to induce long-lasting immunity in adults. Efforts to convert this TI-2 type vaccine into a T dependent vaccine ape being actively pursued and include conjugate vaccine development. Alternatively, the meningococcal polysaccharide can be rendered into a T dependent antigen through the use of peptides which mimic the capsular polysaccharide complexed or conjugated to potent protein carrier molecules. We have previously developed an anti-idiotypic **monoclonal** antibody (**mAb**) based peptide mimic of meningococcal group C polysaccharide (MCPS). A direct approach to identification of peptide mimics of antigen is through the use of peptide display libraries. We have utilized a phage library and a **mAb** with specificity for meningococcal group A polysaccharide (MAPS) to screen for a peptide mimic of MAPS. Six different peptide motifs were selected with the use of the **mAb**. Thirty-eight of the 60 sequenced phage clones were represented by motif 1 and 2 which differed only in three amino acids at the carboxy terminus. Immunological assays were performed. Phage clones with motif 1 and 2 were capable of binding human hyperimmune sera and inhibiting the binding of human hyperimmune sera to nominal antigen. Immunization with motif 1 peptide complexed to proteosomes resulted in an anti-MAPS antibody response. Priming with the peptide proteosome complex induced an anamnestic response indicating the formation of immunological memory. (C) 2000 Elsevier Science Ltd. All rights reserved.

16/3,AB/6 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

10747269 References: 38
TITLE: Baculovirus expression, purification and evaluation of recombinant pneumococcal surface adhesin A of Streptococcus pneumoniae
AUTHOR(S): De BK (REPRINT); **Sampson JS; Ades EW;** Johnson SE; Stinson AR; Crook J; **Tharpe JA;** Huebner RC; **Carlone GM**
AUTHOR(S) E-MAIL: bkd1@cdc.gov
CORPORATE SOURCE: Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, MS

G05,1600 Clifton Rd NE/Atlanta//GA/30333 (REPRINT); Ctr Dis Control & Prevent, Div Bacterial & Mycot Dis, /Atlanta//GA/30333; Pasteur Merieux Connaught Labs Inc, /Swiftwater//PA/
PUBLICATION TYPE: JOURNAL
PUBLICATION: PATHOBIOLOGY, 1999, V67, N3 (MAY-JUN), P115-122
GENUINE ARTICLE#: 214QF
PUBLISHER: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND
ISSN: 1015-2008
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Pneumococcal surface adhesin A (PsaA), with a molecular mass of similar to 37 kD by SDS-PAGE, is a common surface protein expressed by all 90 serotypes of Streptococcus pneumoniae. S. pneumoniae serotype 6B genomic DNA was amplified to generate a DNA fragment carrying the full-length psaA sequence and was cloned into a baculovirus expression system. We expressed either cell-associated or cell-free nonfusion PsaA polypeptides using two insect cell lines, Spodoptera frugiperda (Sf9) and Trichoplusia ni 5B1-4 (High-Five). Recombinant PsaA (rPsaA) polypeptides were partially purified by partitioning in PBS/Triton X-114 buffers and by weakly basic ion exchange filter chromatography. Membrane-bound 'hydrophobic rPsaA' (hrPsaA) expressed by either Sf9 or High-Five cells had a molecular mass of similar to 38 kD by SDS-PAGE and partitioned in a Triton X-114 phase, it reacted with both rabbit polyclonal and five **monoclonal** anti-PsaA antibodies by dot blot or Western blot analysis.

16/3,AB/7 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

09277342 References: 50
TITLE: Immunoreactivity of five **monoclonal** antibodies against the 37-kilodalton common cell wall protein (PsaA) of Streptococcus pneumoniae
AUTHOR(S): Crook J; **Tharpe JA**; Johnson SE; Willlams DB; Stinson AR; Facklam RR; **Ades EW; Carlone GM; Sampson JS (REPRINT)**
CORPORATE SOURCE: CTR DIS CONTROL & PREVENT,DIV BACTERIAL & MYCOT DIS, NATL CTR INFECT DIS, US DEPT HHS/ATLANTA//GA/30333 (REPRINT); CTR DIS CONTROL & PREVENT,DIV BACTERIAL & MYCOT DIS, NATL CTR INFECT DIS, US DEPT HHS/ATLANTA//GA/30333
PUBLICATION TYPE: JOURNAL
PUBLICATION: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, 1998, V5, N2 (MAR), P205-210
GENUINE ARTICLE#: ZA823
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171
ISSN: 1071-412X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Five **monoclonal** antibodies (**MAbs**) were produced against the Streptococcus pneumoniae pneumococcal surface adhesin A (PsaA) 37-kDa common cell wall protein. These antibodies were used in a dot immunoblot and Western blot study of clinical isolates of S. pneumoniae to detect the presence of the protein. By both assays, the **MAbs** reacted with clinical isolates representing the 23 type-specific serotypes present in the licensed pneumococcal polysaccharide vaccine. Western blot analysis

confirmed the presence of a protein migrating in the gel with a molecular mass of 37 kDa. An extension of the study by using dot immunoblot analysis that included an analysis of the 90 serotypes of S. pneumoniae showed that all five **MAbs** reacted with 89 of the 90 serotypes tested. **MAb** 1B6, the exception, did not react with S. pneumoniae serotype 16F. Dot immunoblot analysis of the **MAbs** with Enterococcus faecalis and viridans streptococci showed varied reactivity patterns, depending on the species. The **MAbs** against the 37-kDa antigen did not react with Escherichia coli, respiratory pathogens, or nonpathogens representing 22 genera and 29 species of bacteria. All five **MAbs** also reacted with five multidrug-resistant strains of S. pneumoniae. In summary, these **MAbs** may be useful for detection of pneumococcal antigen and may lead to the development of diagnostic assays for pneumococcal disease.

16/3,AB/8 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
(c) 2005 Inst for Sci Info. All rts. reserv.

02694305 References: 24
TITLE: IMMUNOLOGIC CHARACTERIZATION AND SPECIFICITY OF 3 **MONOCLONAL** ANTIBODIES AGAINST THE 58-KILODALTON PROTEIN OF LEGIONELLA-PNEUMOPHILA
AUTHOR(S): **SAMPSON JS**; PLIKAYTIS BB; ALOISIO CH; **CARLONE GM**; PAU CP; STINSON AR
CORPORATE SOURCE: CTR DIS CONTROL,CTR INFECT DIS,DIV BACTERIAL DIS/ATLANTA//GA/30333 (Reprint); CTR DIS CONTROL,CTR INFECT DIS,DIV HIV AIDS/ATLANTA//GA/30333; CTR DIS CONTROL,CTR INFECT DIS,DIV IMMUNOL ONCOL & HEMATOL DIS/ATLANTA//GA/30333
PUBLICATION: JOURNAL OF CLINICAL MICROBIOLOGY, 1991, V29, N4 (APR), P 836-841
GENUINE ARTICLE#: FC919
LANGUAGE: ENGLISH DOCUMENT TYPE: NOTE

ABSTRACT: Three **monoclonal** antibodies against the Legionella pneumophila 58-kDa protein were produced. By using immunoblot analysis, the percentages of reactivity against 47 serogroups of Legionella representing 29 species were determined to be 80.9, 87.2, and 95.6 for **monoclonal** antibodies GB5BE8, GB5AF6, and CA4AF5, respectively. Specificities obtained from testing 63 heterologous organisms representing 22 genera and 46 species were 90.7, 92.2, and 95.3% for **monoclonal** antibodies GB5BE8, GB5AF6, and CA4AF5, respectively. No single heterologous strain was reactive with all three **monoclonal** antibodies. These **monoclonal** antibodies successfully identified all 10 clinical isolates of Legionella examined in a dot blot assay and should be excellent reagents for use in genuswide diagnostic immunoassays.

16/3,AB/9 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 2005 European Patent Office. All rts. reserv.

01087862
EPITOPE PEPTIDES IMMUNOGENIC AGAINST STREPTOCOCCUS PNEUMONIAE
EPITOPE PEPTIDEN, DIE IMMUNOGENES GEGEN STREPTOCOCCUS PNEUMONIAE SIND
PEPTIDES EPITOPES IMMUNOGENES CONTRE L'INFECTION PAR $i(STREPTOCOCCUS PNEUMONIAE)

PATENT ASSIGNEE:
The Government of the United States represented by the Secretary of the Department of Health and Human Services, (2121783), The Centers for Disease Control and Prevention, Room 500, 255 East Paces Ferry Road N.E., Atlanta, GA 30333, (US), (Applicant designated States: all)
INVENTOR:
CARLONE, George, M., 5243 Sandy Shoals Lane, Stone Mountain, GA 30087, (US)
ADES, Edwin, W., 4432 Whitewater Creek Road, Atlanta, GA 30327, (US)
SAMPSON, Jacquelyn, S., 4220 Greentree Lane, College Park, GA 30349 , (US)
THARPE, Jean, A., 2669 Sherman Oaks Drive, Lithonia, GA 30058, (US)
ZEILER, Joan, Louise, 4322 N. Lockwood, Toledo, OH 43612, (US)
WESTERINK, Maria, Anna, Julia, 8248 Country Brook Drive, Holland, OH 43528, (US
LEGAL REPRESENTATIVE:
HOFFMANN - EITLE (101511), Patent- und Rechtsanwalte Arabellastrasse 4, 81925 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1060249 A1 001220 (Basic)
WO 9945121 990910
APPLICATION (CC, No, Date): EP 99908543 990226; WO 99US4326 990226
PRIORITY (CC, No, Date): US 76565 980302
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; C07K-014/315; C07K-007/08; A61K-038/10; A61K-039/09; G01N-033/566
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

16/3,AB/10 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0288937 DBR Accession No.: 2002-10784 PATENT
New multiple antigenic peptide for immunizing against streptococcal infections, binds to **monoclonal** antibody obtained in response to immunizing an animal with pneumococcal surface adhesion protein A or its fragment - Streptococcus pneumoniae antigen protein production and purification, useful for recombinant vaccine against bacterium infection and for therapy
AUTHOR: **ADES E W**; JOHNSON S E; JUE D L; **SAMPSON J S**; **CARLONE G M**
PATENT ASSIGNEE: US DEPT HEALTH and HUMAN SERVICES 2002
PATENT NUMBER: WO 200204497 PATENT DATE: 20020117 WPI ACCESSION NO.: 2002-195762 (200225)
PRIORITY APPLIC. NO.: US 613092 APPLIC. DATE: 20000710
NATIONAL APPLIC. NO.: WO 2001US21626 APPLIC. DATE: 20010710
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - A multiple antigenic peptide (I) that immunospecifically binds to a **monoclonal** antibody obtained in response to immunizing an animal with Streptococcus pneumoniae pneumococcal surface adhesion protein A (PsaA) or its immunogenic fragment, is new. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also

included for conferring protective immunity against S. pneumoniae infection in a subject comprising administering a therapeutic composition containing (I).WIDER DISCLOSURE - Also disclosed are: (1) a vaccine or therapeutic composition comprising (I) for eliciting an immune response which confers protective immunity against the streptococcal infection; (2) an isolated polynucleotide (II) encoding a 37 kDa protein of S. pneumoniae or its allelic variant; (3) a purified polypeptide (III) or its fragments encoded by (II), useful for detecting the presence of S. pneumoniae in a subject; (4) a purified antibody which selectively binds to (III) or its fragments; and (5) a therapeutic composition comprising (III) or a unique fragment of at least 10 nucleotides of (II). BIOTECHNOLOGY - Preferred Peptide: (I) preferably has an arm comprising a peptide of sequence selected from (P1) - (P6) or an immunogenic fragment of them, more preferably a first arm comprising P1, and a second arm comprising P2 or P5 (bipeptide) and optionally a third arm comprising P3 or P6 (tripeptide), where (I) is lipidated preferably with monopalmitic acid. Thr Val Ser Arg Val Pro Trp Thr Ala Trp Ala Phe His Gly Tyr (P1) Arg Ser Tyr Gln His Asp Leu Arg Ala Tyr Gly Phe Trp Arg Leu (P2) Leu Val Arg Arg Phe Val His Arg Arg Pro His Val Glu Ser Gln (P3) Leu Val Arg Arg Phe Val His His Arg Pro His Val Glu Ser Gln (P4) Leu Val Arg Arg Phe Val His Arg Pro His Val Glu Ser Gln Lys (P5) Ser Tyr Gln His Asp Leu Arg Ala Tyr Gly Phe Trp Arg Leu Lys (P6) ACTIVITY - Antibacterial. MECHANISM OF ACTION - Vaccine. (I) was tested for protection against challenge with a virulent capsular type 3 S. pneumoniae strain, WU2. Twenty CB A/CaHN/J mice carrying the xid mutation (x-linked immunodeficiency) were anesthetized and bled infraorbitally to obtain pre-immunization sera. A 37 kDa protein (pneumococcal surface adhesion A) was emulsified in complete Freund's adjuvant (CFA) to a protein concentration of 54 micrograms/ml. Ten mice were injected subcutaneously into 2 axillary and 2 lingual sites at 0.1 ml/site, delivering approximately 22 microg protein/mouse. Ten control mice were treated identically with CFA and buffer substituting for protein. Fourteen days later, the 10 test mice were injected intraperitoneally (IP) with 100 microg of the 37 kDa protein and controls were injected IP with buffer. Eight days following the IP immunizations, all mice were bled infraorbitally to obtain post-immunization sera, and challenged intravenously (IV) with 60 colony forming units (cfu) of a log phase culture of S. pneumoniae strain WU2. Mice were observed for 21 days, and deaths were recorded. Sera were collected prior to immunizations to establish baseline exposures, and also following the full immunization protocol in order to correlate circulating antibody to the 37 kDa protein with protection. Results showed that 10/10 mice immunized with 37 kDa protein survived and 2/10 mice (controls) with no protein survived (8/10 died). USE - (I) is useful for conferring protective immunity against S. pneumoniae infection in a subject (claimed). ADMINISTRATION - (I) is administered by oral, sublingual, or parenteral routes including intravenous, subcutaneous, intramuscular, mucosal, and inhalation. Dosage of (I) is 1 microg - 10 mg (preferably 50 - 500 microg). EXAMPLE - **Monoclonal** antibodies (I) were produced. Streptococcus pneumoniae DNA digested with restriction enzyme Sau3A1 was ligated to BamHI digested pUC13 and transformed into Escherichia coli TB1. Recombinant clones were identified by colonary immunoblot using the 37 kDa **monoclonal** antibody. The plasmid pSTR3-1 was an example of the pneumococcal surface adhesion A gene cloned into pUC13. Pneumococcal surface adhesion protein A (PsaA) for use as an antigen or

immunogen was purified using any know method for protein purification. A phage display library containing inserts of 15 amino acid residues located at the N-terminal part of the pIII coat protein was constructed in the phage FUSE 5 as the vector. The library was made by ligating a synthetic 33 base pair (bp) BgII fragment into FUSE 5 and transfecting E. coli Kq11/kan+ cells by electroporation The phage progeny contained the display library. 4 cycles of biopanning were carried out for each of (I) employed in order to screen the phage display library for PsaA epitopic peptides. The phage library (1011 to 1012 transforming units) was then incubated with the immobilized (I). Bound phage were eluted from the streptavidin-coated plates with 0.1 N HCl, pH 2.2. The eluted phage were titrated and amplified, and then subjected to two further rounds of selection performed as above. The amount of biotinylated (I) used in the second and third rounds, was such that only high affinity peptides were bound by the end of the last cycle. High-affinity peptides from the library obtained using the above procedures were propagated and sequenced. For each (I), ten phage specimens resulting from the selection process were sequenced. They were compared to known sequences of PsaA strains 2 and 6B using Clusta IV and tFasta programs to identify the epitope on the PsaA with which each peptide was aligned most closely. The peptide obtained using **monoclonal** antibodies 8G12, 6F6, and 1E7 aligned to PsaA best when an additional residue was present on the protein where a gap appeared after residue 13 of the peptide. (85 pages)

16/3,AB/11 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0243753 DBR Accession Number: 1999-14518 PATENT
New peptides corresponding to Streptococcus pneumoniae PsaA, used for treating or preventing Streptococcus pneumoniae infection in a subject - phage FUSE-5-mediated gene transfer and expression in Escherichia coli to create a phage DNA library
AUTHOR: **Carlone G M; Ades E W; Sampson J S; Tharpe J A; Zeiler J L; Westerink M A J**
CORPORATE SOURCE: Atlanta, GA, USA.
PATENT ASSIGNEE: U.S.Dep.Health-Hum.Serv. 1999
PATENT NUMBER: WO 9945121 PATENT DATE: 19990910 WPI ACCESSION NO.: 1999-540849 (1945)
PRIORITY APPLIC. NO.: US 76565 APPLIC. DATE: 19980302
NATIONAL APPLIC. NO.: WO 99US4326 APPLIC. DATE: 19990226
LANGUAGE: English
ABSTRACT: Peptides that immunospecifically bind to a **monoclonal** antibody (**MAb**) obtained in response to immunizing an animal with Streptococcus pneumoniae (SP) pneumococcal surface adhesion-A protein (PsaA) are new. Also claimed are: a peptide produced by providing a library of random oligonucleotides, splicing the oligonucleotides into the gene for gene-III coat protein of a filamentous phage (e.g. phage FUSE-5) to create a phage library, expanding the phage library by culturing in a host (e.g. Escherichia coli Kq1/kan+), screwing the expanded library for a specific phage particle that immunospecifically reacts with a **MAb** obtained in response to immunizing an animal with SP PsaA and sequencing the gene for the coat protein of the phage obtained; a therapeutic composition containing one or more peptides

produced; and a peptide containing a sequence at least 80% identical to defined peptides. The peptides can be used for treating or preventing infection by SP in a subject. (58pp)

16/3,AB/12 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0219746 DBR Accession Number: 98-01343
Baculo virus expressed recombinant pneumococcal surface adhesin-A (rPsaA) of Streptococcus pneumoniae serotype 6B - generates murine antibodies capable of passive protection in an infant mouse model of bacteremia; polyclonal, **monoclonal** antibody generation (conference abstract)
AUTHOR: De B K; Johnson S E; **Ades E W**; Stinson A R; Crook J; Huebner R C; **Sampson J S**; **Carlone G M**
CORPORATE AFFILIATE: Connaught-Lab. Cent.Dis.Contr.Prev.Atlanta
CORPORATE SOURCE: Connaught Laboratories, Inc., Swiftwater, PA, USA.
JOURNAL: Abstr.Gen.Meet.Am.Soc.Microbiol. (97 Meet., 251) 1997
ISSN: 0067-2777 CODEN: 0005P
CONFERENCE PROCEEDINGS: American Society for Microbiology, 97th General Meeting, Miami Beach, FL, 4-8 May, 1997.
LANGUAGE: English
ABSTRACT: Pneumococcal surface adhesin-A (PsaA) from Streptococcus pneumoniae serotype 6B was expressed in Spodoptera frugiperda Sf9 and Trichoplusia ni High Five insect cell culture using the baculo virus expression system. Recombinant PsaA was partially purified by partitioning in phosphate buffered saline/Triton X-114 buffer and by D5 ionexchange filter chromatography. PsaA was expressed as an Sf9 cell-associated protein with a mol.weight of 38,000, which partitioned in the Triton X-114 phase, and reacted with rabbit polyclonal and **monoclonal** antibodies by dot blot and Western blot analysis. High Five cells expressed PsaA in serum-free culture medium as a cell-free soluble protein with a mol.weight of 37,000, which did not partition in the Triton X-114 phase, and reacted with polyclonal and **monoclonal** antibodies by ELISA and Western blot analysis. PsaA was immunogenic in Swiss-Webster adult female mice. Anti-PsaA immune serum was used for passive immunization in infant mouse bacteremic models. (0 ref)

16/3,AB/13 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.
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0168982 DBR Accession Number: 94-11533
The utility of recombinant protein in an enzyme immunoassay for antibodies against Streptococcus pneumoniae - recombinant pneumococcal surface adhesin A antigen production, purification, characterization and application in pneumococcal disease diagnosis (conference abstract)
AUTHOR: **Tharpe J A**; **Sampson J S**; Stinson A R; Russel H
CORPORATE AFFILIATE: CDC
CORPORATE SOURCE: CDC, Atlanta, GA 30333, USA.
JOURNAL: Abstr.Gen.Meet.Am.Soc.Microbiol. (94 Meet., 617) 1994
CODEN: 0005P
LANGUAGE: English

ABSTRACT: Most pneumococcal diagnostic assays lack sensitivity and specificity. A 37 kDa pneumococcal surface adhesin A (PsaA) shows promise as a diagnostic. To augment production, the gene encoding PsaA was cloned into expression vector plasmid pMal-cTM. The expressed protein was a maltose-binding fusion protein due to insertion of psaA downstream from the vector malE gene. The fusion protein was purified by affinity chromatography and analyzed by SDS-PAGE to determine purity and confirm migration at the expected approximate mol.weight of 70,000. The immunoreactivity of the purified fusion protein was evaluated using polyclonal and **monoclonal** antibody to native PsaA. The ability to utilize recombinant protein as a replacement solid-phase antigen for native protein was investigated by ELISA. Bacteremic sera from 25 patients diagnosed with pneumococcal disease were tested with both native protein and recombinant protein. Test results indicated that the fusion protein can serve as a useful substitute for native pneumococcal protein in the ELISA. (0 ref)

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RESULT 1
US-09-613-092A-6
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; APPLICANT: Ades, Edwin W.
; APPLICANT: Sampson, Jacquelyn S.
; APPLICANT: Tharpe, Jean A.
; APPLICANT: Johnson, Scott E.
; APPLICANT: Jue, Danny L.
; APPLICANT: Carlone, George M.
; APPLICANT: Zeiler, Joan L.
; APPLICANT: Westerlink, Maria Anna J.
; TITLE OF INVENTION: Multiple Antigenic Peptides Immunogenic
; TITLE OF INVENTION: Against Streptococcus Pneumonia
; FILE REFERENCE: 14114.0341U1
; CURRENT APPLICATION NUMBER: US/09/613,092A
; CURRENT FILING DATE: 2000-07-10
; NUMBER OF SEQ ID NOS: 10
; SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 6
; LENGTH: 15
; TYPE: PRT
; ORGANISM: Artificial Sequence
; FEATURE:
; OTHER INFORMATION: Description of Artificial Sequence; note =
; OTHER INFORMATION: synthetic construct
US-09-613-092A-6

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Best Local Similarity 100.0%; Pred. No. 1.5e-09;
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Db 1 RSYQHDLRAYGFWRL 15

RESULT 2
US-09-613-092B-6
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; GENERAL INFORMATION: